Immunodeficient mice are better for modeling the transfusion of human blood components than wild-type mice.

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Public Summary:
Animal models are vital to the study of transfusion and development of new blood products. Post-transfusion recovery of human blood components can be studied in mice, however, there is a need to identify strains that can best tolerate xenogeneic transfusions, as well as to optimize such protocols. Specifically, the importance of using immunodeficient mice, such as NOD.Cg-Prkdcscid Il2rgtm1Wjl/SzJ (NSG) mice, to study human transfusion has been questioned. In this study, strains of wild-type and NSG mice were compared as hosts for human transfusions with outcomes quantified by flow cytometric analyses of CD235a+ erythrocytes, CD45+ leukocytes, and CD41+CD42b+ platelets. Complete blood counts were evaluated as well as serum cytokines by multiplexing methods. Circulating human blood cells were maintained better in NSG than in wild-type mice. Lethargy and hemoglobinuria were observed in the first hours in wild-type mice along with increased pro-inflammatory cytokines/chemokines such as monocyte chemoattractant protein-1, tumor necrosis factor alpha, keratinocyte-derived chemokine (KC or CXCL1), and interleukin-6, whereas NSG mice were less severely affected. Whole blood transfusion resulted in rapid sequestration and then release of human cells back into the circulation within several hours. This rebound effect diminished when only erythrocytes were transfused. Nonetheless, human erythrocytes were found in excess of mouse erythrocytes in the liver and lungs and had a shorter half-life in circulation. Variables affecting the outcomes of transfused erythrocytes were cell dose and mouse weight; recipient sex did not affect outcomes. The sensitivity and utility of this xenogeneic model were shown by measuring the effects of erythrocyte damage due to exposure to the oxidizer diamide on post-transfusion recovery. Overall, immunodeficient mice are superior models for xenotransfusion as they maintain improved post-transfusion recovery with negligible immune-associated side effects.

Scientific Abstract:
Animal models are vital to the study of transfusion and development of new blood products. Post-transfusion recovery of human blood components can be studied in mice, however, there is a need to identify strains that can best tolerate xenogeneic transfusions, as well as to optimize such protocols. Specifically, the importance of using immunodeficient mice, such as NOD.Cg-Prkdcscid Il2rgtm1Wjl/SzJ (NSG) mice, to study human transfusion has been questioned. In this study, strains of wild-type and NSG mice were compared as hosts for human transfusions with outcomes quantified by flow cytometric analyses of CD235a+ erythrocytes, CD45+ leukocytes, and CD41+CD42b+ platelets. Complete blood counts were evaluated as well as serum cytokines by multiplexing methods. Circulating human blood cells were maintained better in NSG than in wild-type mice. Lethargy and hemoglobinuria were observed in the first hours in wild-type mice along with increased pro-inflammatory cytokines/chemokines such as monocyte chemoattractant protein-1, tumor necrosis factor alpha, keratinocyte-derived chemokine (KC or CXCL1), and interleukin-6, whereas NSG mice were less severely affected. Whole blood transfusion resulted in rapid sequestration and then release of human cells back into the circulation within several hours. This rebound effect diminished when only erythrocytes were transfused. Nonetheless, human erythrocytes were found in excess of mouse erythrocytes in the liver and lungs and had a shorter half-life in circulation. Variables affecting the outcomes of transfused erythrocytes were cell dose and mouse weight; recipient sex did not affect outcomes. The sensitivity and utility of this xenogeneic model were shown by measuring the effects of erythrocyte damage due to exposure to the oxidizer diamide on post-transfusion recovery. Overall, immunodeficient mice are superior models for xenotransfusion as they maintain improved post-transfusion recovery with negligible immune-associated side effects.

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